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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/752,423	01/06/2004	Erik Buntinx	29248/19	3783

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
05/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/752,423	BUNTINX, ERIK	
	Examiner	Art Unit	
	UMAMAHESWARI RAMACHANDRAN	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *04 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,9 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/11/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner notes the receipt of the amendments and remarks received in the office on 2/4/2008. Claims 1, 7, 9, 10 have been amended and claims 2-6, 8, 11-63 have been canceled. Claims 1, 7, 9, 10 are currently pending and are being examined on the merits herein.

Response to Remarks

Applicants' acknowledges the provisional rejection of claims 1-4, 6-9 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 42 of copending Application No. 10/984,683 and claims 1-4, 6-10 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 82-84, 100, 101 of copending Application No. 10/580,962. The rejections are maintained and modified version of the rejections (due to the amendments) is given below for Applicants' convenience. Applicants' have not put forth any arguments regarding the 35 U.S.C 112(1) rejections. The rejection of claims 1-4, 6-10 under 35 U.S.C. 112, first paragraph (written description), the rejection of claims 1-4, 6-10 under 35 U.S.C. 112, first paragraph, enablement for anxiety disorder is maintained and modified rejections have been made due to the amendment of claims and are provided below. Applicants' arguments regarding the rejection of claims 1-4, 6-10 under 35 U.S.C. 103(a) as being unpatentable over Dudley et al. (US 2004/0002482) in view of Dodman (U.S. 5,762,960) and further in view of Sanchez (U.S. 2002/0086899) have been fully considered and found to be persuasive and hence the rejection is withdrawn.

Further search and consideration necessitated the new rejections presented in this office action. Hence the action is made non final.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 42 of copending Application No. 10/984,683 in view of in view of Sanchez (U.S. 2002/0086899).

Claims 1 and 9 of the instant application is drawn to a method of for treating a disease or disorder such as anxiety disorder comprising administering to a patient a compound such as pipamperone and a second agent such as serotonin reuptake inhibitor.

Claims 1-4 and 42 of co-pending application ('683) teach a method for treating a disease or disorder with an underlying dysregulation of the emotional functionality that include anxiety disorders, mood disorders etc. comprising, administering to a patient pipamperone simultaneously with, separate from or sequential to second compound to

augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said second compound. The application teaches that second compound can be a selective serotonin reuptake inhibitor.

The co-pending application does not teach the selective serotonin reuptake inhibitor to be citalopram.

Sanchez teach the use of escitalopram (s-enantiomer of citalopram, 40 mg/kg) in the treatment of neurotic disorders including anxiety disorder, social anxiety disorder etc. (See Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to administer pipamperone along with citalopram in a method of treating anxiety disorder because Sanchez et al. teach citalopram, an SSRI compound is effective in the treatment of social anxiety disorder. One having ordinary skill in the art at the time of the invention would have been motivated to add citalopram as a second agent in a method of treating anxiety disorder along with pipamperone in expectation of success and in expectation of synergistic and additive effects.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both teach a method of treatment of emotional disorders such as anxiety disorder comprising administering pipamperone and a selective serotonin reuptake inhibitor as a second agent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 9,10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 82-84, 100, 101 of copending Application No. 10/580,962.

Claims 1, 9 and 10 of the instant application are drawn to a method of for treating a disease or disorder such as anxiety disorder comprising administering to a patient a compound such as pipamperone and a second agent, citalopram, a serotonin reuptake inhibitor.

Claims 82-84, 100,101 of the co-pending application ('962) teach a method for treating mood disorders or anxiety disorders comprising administering to a patient pipamperone, or a pharmaceutically acceptable salt thereof, in a dose ranging between 5 and 15 mg per day of the active ingredient, and administering said pipamperone simultaneously with, separate from or sequential to a second compound, to augment the therapeutic effect of said second compound or to provide a faster onset of the therapeutic effect of said second compound, wherein said second compound is selected from the group consisting of: selective serotonin, nor-adrenaline and dopamine re-uptake inhibitors (SNDRI), selective serotonin and nor-adrenaline re-uptake inhibitors (SNRI) and selective serotonin re-uptake inhibitors (SSRI). The co-pending application further teaches escitalopram, fluoxetine etc to be a second agent.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both teach a method of treatment of emotional disorders such as anxiety disorder comprising administering pipamperone and a selective serotonin reuptake inhibitor such as citalopram as a second agent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 7, 9, 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The specification teach measuring pKi values of some test compounds and describes the foregoing pipamperone-citalopram treatment for depressive disorder clinical trial set up data but do not show any real data or examples of treating a disorder such as anxiety disorder administering to a patient a compound such as pipamperone and citalopram. Also, there is no data in the specification showing the augmentation of therapeutic effect of SSRI or a faster onset of the therapeutic effect of said SSRI when the selective serotonin reuptake inhibitor is administered to the patient simultaneously with, separate from or sequential to the administration of pipamperone. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not provide support to the subject matter of the claimed invention of treating a disease or a disorder with an underlying dysregulation of the emotional functionality comprising administering a compound that

has selective affinity for dopamine D4 receptor and a selective affinity for 5-HT2A receptor.

Claims 1, 7, 9, 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification teach measuring pKi values of some test compounds and describes the foregoing pipamperone-citalopram treatment for depressive disorder clinical trial set up data does not reasonably provide enablement for anxiety disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.
The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the Invention and (2) Breadth of the claims:

The rejected claims are drawn to a method of treating anxiety disorder, comprising administering pipamperone in a dose ranging from 5 and 15 mg and a

selective serotonin re-uptake inhibitor (SSRI) to augment the therapeutic effects of SSRI compound. Claim 1 is limited to anxiety disorder but the claims is broad as it is drawn to a method treating anxiety disorder with pipamperone and a selective serotonin re-uptake inhibitor (SSRI). A huge number of compounds fall under the category of SSRI which includes the known and unknown compounds and the claims teach a combination of therapy of pipamperone with each and every single SSRI compound. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims as it teaches a method treating anxiety disorder with pipamperone and addition of a second agent an SSRI compound to augment the therapeutic effects of SSRI.

(3) Guidance of the Specification:

The guidance given by the specification is for measuring pKi values of some test compounds and description of the foregoing pipamperone-citalopram treatment for depressive disorder clinical trial set up.

(4) Working Examples:

The specification provides set up data for the clinical trial for a method of treatment of depressive disorder.

(5) The relative skill of those in the art:

The relative skill of those in the medical treatment art is high, requiring advanced education and training.

(6) The predictability of art:

The method claim is directed to the treatment of anxiety disorder with pipamperone and a second agent SSRI added simultaneously with, separate from or

sequential to the administration of pipamperone to augment the therapeutic effect of said SSRI to provide faster onset of the therapeutic effect of said SSRI is broad and there is a high degree of unpredictability involved. The specification does not provide any combination therapy comprising administering pipamperone and an SSRI agent in a method of treatment of anxiety and in addition there is no teaching in the specification to show the augmentation of the therapeutic effects of SSRI agent administered along with pipamperone. Despite the advanced training in the medical treatment arts, the arts are highly unpredictable.

(7) The Quantity of Experimentation Necessary:

In order to practice the above claimed invention, one of skill in the art would have to first envision formulation, dosage, duration, route and, in the case of human treatment, an appropriate animal model system to test every single combination of pipamperone and SSRI agents and for the augmentation effects of SSRI agent administered simultaneously or sequentially with pipamperone in a method of treatment of anxiety. If unsuccessful, one of skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of the treatment of anxiety disorder with pipamperone and a second agent SSRI wherein SSRI is added simultaneously with, separate from or sequential to the administration of pipamperone to augment the therapeutic effect of said SSRI to provide faster onset of the therapeutic effect of said SSRI. Genetech, 108 F.3d at 1366

states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 7, 9, 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dipiperon (Applicant cited IDS reference, manufacturer sheet) in view of Sanchez (U.S. 2002/0086899).

Dipiperon document teaches that pipamperone (dipiperon) is useful in the symptomatic treatment of serious forms of agitation and anxiety (p 1, Therapeutic indications). The reference teaches 40-80 mg doses for adults and 20 mg divided in two doses for children.

The reference does not teach a combination therapy with an SSRI such as citalopram in a method of treatment of anxiety.

Sanchez teach the use of escitalopram (s-enantiomer of citalopram, 40 mg/kg) in the treatment of neurotic disorders including anxiety disorder, social anxiety disorder etc. (See Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use pipamperone and citalopram in a method of treatment of a disease or a disorder such as anxiety disorder because of the teachings of Dipiperon and Sanchez. Diperon teaches the use of pipamperone in the treatment of anxiety disorder and Sanchez teaches the use of citalopram in the treatment of anxiety disorders. Hence one of ordinary skill in the art would have been motivated to use pipamperone and citalopram in a combination therapy for the treatment of a disease or a disorder such as anxiety disorder due to expectation of synergistic effects and therapeutic benefits as both the compounds have been shown to be useful in a method of treatment of condition like anxiety disorder. Regarding the daily dose of pipamperone in the composition as recited in claim 1 Dipiperon teach a dose of 10 mg to children (20 mg/day divided in two doses). Also, It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 223,235 (CCPA 1955).

The references do not teach the administration of SSRI as simultaneous or sequential and pipamperone augments the therapeutic effect of said SSRI. It would

have been obvious to one of ordinary skill in the art at the time of the invention that drugs useful for the same disorder or disease can be given as a combination therapy and it is well known that in combination therapy drugs are administered simultaneously or sequentially as the prior art (Dudley et al. (US 2004/0002482)) teaches citalopram and pipamperone can be used in combination therapy in a method of treatment of depressive disorder. Accordingly in a combination therapy of pipamperone and citalopram when SSRI is administered sequentially or simultaneously after administration of pipamperone the effects will be the same as claimed (augmentation of therapeutic effects of SSRI).

Response to Arguments

Applicant's arguments with respect to the 103 (a) rejection of the claims have been considered but are moot in view of the new grounds of rejection. Applicants' have not put forth any arguments regarding the 35 U.S.C 112(1) rejections. The rejection of claims 1-4, 6-10 under 35 U.S.C. 112, first paragraph (written description), the rejection of claims 1-4, 6-10 under 35 U.S.C. 112, first paragraph, enablement for anxiety disorder is maintained and modified rejections have been made due to the amendment of claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to UMAMAHESWARI RAMACHANDRAN whose

telephone number is (571)272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SREENI PADMANABHAN/
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